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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/912,609	07/25/2001	Evan C. Unger	UNGR-1599	8279

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EXAMINER	
SHAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/912,609	Applicant(s) UNGER ET AL.	
	Examiner Shahnam Sharareh	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/25/01, 8/4/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-100* is/are pending in the application.

4a) Of the above claim(s) *7,10,11,21-39 and 43-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,12-20 and 40-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/703,484.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/3/01, 2/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 1-48 in the reply filed on May 26, 2004 is acknowledged. Applicant's election of species of polyethylene glycol-polycaprolactone copolymers, camptothecin, and CRGDC are also acknowledged. Claims 1-6, 8-9, 12-20, 40-42 read on the elected species. The search was also expanded to capture other polymeric targeted matrix wherein the polymer is of polyethylene glycol or poly(lactic-co-glycolic acid). Thus the claims are examined to the extent they read polyethylene glycol-polycaprolactone copolymers (PEG-PCL), polyethylene glycol (PEG) or poly(lactic-co-glycolic acid) (PLGA) as the polymeric matrix; camptothecin as the bioactive agent; and CRGDC as the targeting ligand.

Claims 7, 10-11, 21-39, 43-48 are withdrawn as they are not directed to the elected species. Claim 49-105 are also withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 26, 2004.

This application contains claims 49-105 drawn to an invention nonelected and claims 7, 10-11, 21-39, 43-48 drawn to nonelected species. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-20 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "limited" in claim 13 is a relative term which renders the claim indefinite. The term "limited" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8, 13, 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Gref et al US Patent 5,543,158 (Gref).

Gref meets the limitations of the instant claims. Gref discloses compositions comprising particles of a solid biodegradable core comprising PEG and PLGA loaded with a chemotherapeutic or immunosuppressive agent. (see col 3, lines 55-60; col 4, lines 45-65; col 12, lines 39-55; col 14, lines 25-65; claims 1-6). The internal solid core of Gref meets the limitations of the instant matrix. Gref states "a wide range of biological active materials or drugs can be incorporated into the polymer at the time of nanoparticle formation." (see col 12, lines 15-17). Gref then exemplified that hydrophobic drugs may be entrapped into the injectable particles (see col 12, lines 43-

45). Gref further states that various types of therapeutic compounds may be incorporated or encapsulated within the internal biodegradable core. (see col 6, lines 1-15). Gref teaches that peptide fragments and/or antibodies can be covalently bounded to the outside of particles. (see col 5, lines 20-30; col 6, lines 26-31; col 18, lines 39-47). Such configuration meets the targeting element of the instant matrix system. Gref also teaches oral or injectable compositions that can be lyophilized which also fall within the scope of the instant matrix. (col 16, lines 30-45). Thus, Gref meets all the limitations of the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 16-20, 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gref in view of Quay EP 0727225 (Quay), Ruoslahti et al US Patent 5,981,478 (Ruoslahti), and Wallace US Patent 5,238,714 (Wallace).

Gref's teachings are discussed above. Gref does not teach the instant targeting ligand CRDG.

Quay, Ruoslathi and Wallace are used to show that polymeric microcapsules are readily attached to a targeting ligand to improve specific targeting to tissue cells of interest.

Quay teaches various ligands that can be conjugated to contrast agents in colloidal dispersions (abstract, page 3, lines 1-20). Such ligands include CAM ligands such as RGD or cyclic molecules including CRGD, which is specific integrins, and CAM ligands (page 7, line 20-page 8, line 62).

Ruoslahti teaches specific targeting ligands such as CRGDC, and that they are more specific than RGD in inhibiting fibronectin attachment to α5 - β1 (abstract; col 8, lines 21-67; col 9, lines 63-67).

Wallace teaches process of conjugating amino acid esters to the surface polymers of microcapsules to provide targeting to specific tissue cells (abstract). The polymeric microcapsules of Wallace can be made of PCL or polylactide (see col 1, lines 6-30; col 9, line 39-col 10, line 60).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to conjugate a specific targeting agent such as CRDGC of Ruoslahti to Gref's microparticles to increase specificity of such particles toward a specific tissue cells by employing conjugation methods described by Quay and Wallace. One of ordinary skill in the art would have made such modifications of polymeric microparticles

of Gref, because he would have had a reasonable expectation of success in enhancing cell specificity and thus enhancing intended therapeutic outcome.

Claims 1-6, 8-9, 12-20, 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter US Patent 6,759,431 (Hunter), in view of Domb et al US Patent 5,578,325 (Domb) and Ruoslahti.

Hunter teaches various forms of polymeric drug delivery systems that may be used for delivery of camptothecin. (Abstract; col 15, line 20; col 74, lines 15-36). The polymeric moieties of Hunter can be in various forms including drug-loaded microspheres or drug loaded polymeric pastes (col 29, line 50-col 31, line 20; col 56, line 50, col 58, line 67). The polymeric moieties of Hunter comprise PCL, PEG or copolymers thereof in the form of diblocks or paste (col 43, lines 10-col 44, lined 20; col 46, lines 5-65; col 56, lines 50-col 57, line 50; col 69, lines 15-65). Hunter explains that the type and concentration of his polymeric carrier can be fashioned to provide a desired release characteristic (col 21, line 46-co 22, line 65). Hunter also teaches targeted drug delivery to improve Hunter's teachings meets the limitations of claims 1-6, 8-9, 12-16. Hunter does not specifically teach the use of CRGDC as a targeting agent to enhance the tissue specificity of its formulations.

Domb teaches that polymeric moieties of PCL or PEG diblock copolymers can be covalently attached to a targeting ligand to enhance their tissue specificity. (col 13, lines 1-15) (col 15, lines 25-line 65; col 21, lines 40-59).

Ruoslahti teaches specific targeting ligands such as CRGDC, and that they are more specific than RGD in inhibiting fibronectin attachment to α5 - β1 (abstract; col 8, lines 21-67; col 9, lines 63-67).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to covalently attach a targeting ligand of choice, such as the CRGDC of Ruoslathi to the polymeric drug delivery systems of Hunter, because as elaborated in the art by Domb, one of ordinary skill in the art would have had a reasonable expectation of success in improving the tissue specificity of Hunter's drug delivery system in modulating α5 - β1 receptor activity.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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